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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,235	09/25/2006	Stephen Robert Wedge	056291-5302	1868

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EXAMINER	
PURDY, KYLE A	

ART UNIT	PAPER NUMBER
1611	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,235	WEDGE, STEPHEN ROBERT	
	Examiner	Art Unit	
	Kyle Purdy	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 October 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *21-24,27,28 and 31-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *21-24,27,28 and 31-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1 page (10/14/2009)*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. The Examiner acknowledges receipt of the arguments filed on 10/14/2009.

2. Claims 21-24, 27, 28 and 31-34 are presented for examination on the merits. The following rejections are made.

Response to Applicants' Arguments

3. Applicants arguments filed 10/14/2009 regarding the rejection of claims 21-24, 27, 28 and 31-34 made by the Examiner under nonstatutory obviousness type double patenting over copending application Nos. 10/563440; 11/663912 in view of Lee (US 2002/0002162) have been fully considered and they are found persuasive. This rejection has been overcome by abandonment of the copending applications.

4. Applicants arguments filed 10/14/2009regarding the rejection of claims 21-24, 27, 28 and 31-34 made by the Examiner under nonstatutory obviousness type double patenting over copending application Nos. 10/563439; 10/594233; 10/594234 in view of Lee (US 2002/0002162) have been fully considered but they are not found persuasive.

5. The rejection of claim 21-24, 27, 28 and 31-34 made by the examiner under nonstatutory obviousness type double patenting is **MAINTAINED** for the reasons of record in the office action mailed on 07/14/2009.

6. In regards to the double patenting rejection, Applicant asserts the following:

A) Applicant cannot respond to this ground of rejection unless and until claims are allowed in the reference applications before allowance of the present application.

7. In response to A, Applicant is essentially stating the rejection be held in abeyance. However, A request to hold a rejection in abeyance is not a proper response to a rejection. Rather, a request to hold a matter in abeyance may only be made in response to an OBJECTION or REQUIREMENTS AS TO FORM (see MPEP 37 CFR 1.111(b) and 714.02). Thus, the double patenting rejections of record have been maintained as no action regarding these rejections has been taken by applicants at this time.

8. Applicants arguments filed 10/14/2009 regarding the rejection of claims 21, 23, 24, 27, 28 and 31-33 made by the Examiner under 35 USC 103(a) over Stokes et al. (WO 00/47212) have been fully considered but they are not found persuasive.

9. Applicants arguments filed 10/14/2009 regarding the rejection of claim 22 made by the Examiner under 35 USC 103(a) over Stokes et al. (WO 00/47212) in further view of Seibert et al. (US 5972986) have been fully considered but they are not found persuasive.

10. Applicants arguments filed 10/14/2009regarding the rejection of claim 34 made by the Examiner under 35 USC 103(a) over Stokes et al. (WO 00/47212), in further view of Oncology Channcel (1999) have been fully considered but they are not found persuasive.

11. The rejection of claims 21-24, 27, 28 and 31-34 made by the examiner under 35 USC 103(a) is **MAINTAINED** for the reasons of record in the office action mailed on 07/14/2009.

12. In regards to the 103(a) rejection, Applicant asserts the following:

B) There is no suggestion or any other motivation in Stokes that would lead an ordinary person to specifically select AZD2171 from among the disclosed antiangiogenic compounds and

to specifically select a platinum agent from the long list of chemotherapeutic agents and to administer the two agents as present claimed;

C) No preference is expressed by Stokes for any particular antiangiogenic and/or vascular permeability reducing agent to use in such a combination therapy. As such researchers would have had to vary "all parameters or try each of numerous possible choices until one possibly arrive[s] ata successful result, where the prior art gives no either no indication of which parameters are ciritical or no direction as to which of many possible choices is likely to be successful";

D) The Examiner has used improper hindsight in formulating the rejection;

E) Seibert fails to provide any teaching that might suggest a combination therapy of AZD2171 and a plantinum anti-tumor agent; and

F) There is no way of knowing the true date of the Onconogy Channel reference.

13. In response to B, this is not persuasive to the Examiner. The invention of Stokes is administering an angiogenesis inhibitor derived from a genus of compounds. From that genus, AZD2171 is taught to be a preferred compound. Thus, any ordinary person would have readily envisaged administering the compound for the treatment of angiogenesis. With respect to administering that compound with other means of treating angiogenesis, radiation and antineopplastic agents, this is suggested by the reference, contrary to Applicants assertion. Page 84 states:

"According to a further feature of the invention there is provided a method for producing an antiangiogenic and/or vascular permeability reducing effect in a warm-blooded animal, such as a human being, in need of such treatment which comprises administering to said animal an effective amount of a compound of formula I or a pharmaceutically acceptable salt thereof as defined hereinbefore…….. The antiangiogenic and/or vascular permeability reducing treatment defined hereinbefore may be applied as a sole therapy or may involve, in addition to a

compound of the invention, one or more other substances and/or treatments. Such conjoint treatment may be achieved by way of simultaneous, sequential, or separate administration of the individual components of the treatment….. In medical oncology the other component(s) of such conjoint treatment is addition to the antiangiogenic agent and/or vascular permeability reducing treatment defined hereinbefore may be surgery, radiotherapy or chemotherapy."

It's clear that the antiangiogenic and/or vascular permeability reducing treatment requires an effective amount of a compound of formula 1, which AZD2171 belongs to and is singled out as preferred. Also, the Examiner acknowledges, as was in the previous office action, that the reference fails to explicitly disclose a method of using AZD2171 with chemotherapy and radiation therapy, still however such a method would have been obvious, especially in light of the above teaching. Any ordinary person could have selected any of the preferred antiangiogenic compounds of formula 1 and administered that compound in conjunction radiation and chemotherapy. If such an undertaking resulted in AZD2171 being administered with a platinum derivative and radiation, then such a result would have been the product of ordinary skill and common sense, as the result would have been obtained by any ordinary person with the ability to read and heed advice and suggestions of the reference.

14. In response to C, as was discussed above, it's acknowledged that AZD2171 is not specifically mentioned for use in the conjunctive therapy. However, as the conjunctive therapy requires the antiangiogenic and/or vascular permeability reducing treatment with a compound of formula 1, any ordinary person could have readily selected AZD2171 with a reasonable expectation for success. With respect to the argument that an ordinary researcher would have had no direction as to which of the many possible combinations would have been successful, this is not persuasive. The conjuctive therapy requires a compound belonging to formula 1 (AZD2171), radiation and an chemotherapeutic antineoplastic agent. Any person of ordinary skill in the art

would have envisaged use of the platinum derivative, as they are specifically recited as useful antineoplastic agents. The only real parameter which would have provided any difficulty in predicting the successful outcome of the method would have been the selection of AZD2171 from the generic formula 1. However, this difficulty is mitigated as AZD2171 is specifically singled out as a preferable antiangiogenic agent. Thus, it is the position of the Examiner that the claimed combination would have been obvious and any ordinary person would have readily expected success upon conceiving/arriving at it.

15. In response to D, Applicant is reminded that 'any judgment on obviousness is in a sense necessarily a reconstruction based on hindsight reasoning, but so long as it takes into account only knowledge which was within the level of ordinary skill in the art at the time the claimed invention was made and does not include knowledge gleaned only from Applicants disclosure, such a reconstruction is proper.' See MPEP 2145 X(A). As all of Applicants claimed limitations were within and suggested by the references at the time the invention was made, the rejection of record did not improperly use hindsight.

16. In response to E, Seiberts does not have to teach a conjunctive therapy comprising AZD2171 and oxaliplatin. Stokes provides this teaching by suggesting a conjunctive therapy with the formula 1 (i.e. AZD2171 genus) and antineoplastic agents (i.e. platinum derivatives). Seibert is relied upon for the teaching that oxaliplatin is a platinum derivative and oxaliplatin would have been obvious to include in the conductive treatment method of Stokes.

17. In response to F, this is not persuasive. At the top of the publication, it's written that the original date of publication was "15 Aug 1999", later being reviewed on 04 Dec 2007. With respect to the page being last modified on 16 Mar 2009, there is no way of knowing what this

modification was. However, it's doubtful that it had anything to do with the body of text regarding the various cancer types as this would have been reflected near the top where the original date of publication and date of last review is posted. Absent any evidence that the modification directly impacted the information presented, Applicants argument is moot.

Maintained Rejections, of Record
Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

18. Claims 21-24 and 27-34 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of copending Application No. 10/563439; 10/594,233; 10/594,234 in view of Lee (US Pub No. 2002/0002162; Pub.Date Jan.3,2002.) The limitation of the claims in the instant application is drawn to AZD2171 combined with a platinum anti-tumor agent. The limitation of the claims of

application 10/563439 is drawn to AZD2171 and ZD1839, which is an anti-tumor agent. Lee '162 , teaches therapies for treatment of cancer , that further, teach a synergistic method for the treatment of cancer in a mammalian specie[0002,0011] which comprises a vascular endothelial growth factor receptor tyrosine kinase inhibitor, ZD6474 [0082],(Also a anti-tumor agent) in conjunction with carboplatin [0079], cisplatin and oxaliplatin [Table 1](platinum anti0tumor agtents) for the treatment of breast, pancreas, bladder colon lung, skin colorectal, non-small cell lung cancer and mesothelioma.[0059-0067]. Lee also teaches of radiation therapy that includes but is not limited to x-rays or gamma rays [0068], that is usually given at the same time as the cancer treating method discussed above. The platinum anti tumor agents (carboplatin, cisplatin, and oxaliplatin) used in the method of Lee '162 can also be added to the VEGF tyrosine kinase inhibitor (AZD2171) of copending Application No. 10/563439. This would be obvious to do so to provide a further cytoxic agents. Copending applications: 10/594,233 and 10/594,234 are also provisionally rejected on the ground of nonstatutory obviousness-type double patenting because their claims can be modified by Lee for the same reasons stated above.

19. This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

22. **Claims 21, 23, 24, 27, 28 and 31-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Stokes et al. (WO 00/47212; published 08/17/2000).**

23. Stokes is directed to quinazoline derivates as angiogenesis inhibitors. Stokes teaches that the instantly claimed compound AZD2171 (4-(4-fluoro-2-methylindol-5-yloxy)-6-methoxy-7-(3-(pyrrolidin-1-yl)propoxy)quinazoline) (see page 57, line 31). The compound may be administered as the compound itself or in the form of a salt (see abstract). The method of treating angiogenesis with the compound of note as well as simultaneously administering radiotherapy and antineoplastic agents such as platinum derivatives like cisplatin and carboplatin (see page 85). It's taught that the radiotherapy and antineoplastic agents may be administered simultaneously, sequentially or separately from administration of the quinazoline derivative (see page 85, lines 1-5). The types of cancers treated by the compounds of Stokes include Kaposi's sarcoma as well as solid tumors such as colorectal and lung cancer (see page 86, lines 11-23).

24. Stokes fails to specifically teach using said compound in a method of treating cancer.

25. Regardless, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the teachings of Stokes with a reasonable expectation for success in arriving at a method of treating cancer in a method of administering AZD2171 before after or

simultaneously with a platinum anti-tumor agent and radiotherapy. Although stoke fails to specifically use the instantly claimed compound in a method of cancer treatment, any person of ordinary skill could have readily identified said compound for use in a method with a reasonable expectation for success in treating the condition. The reference teaches that AZD2171 is a more preferred compound for use in such treatments. Thus, it would not have been innovative to pick a compound that had been suggested for cancer treatment as the currently claimed method does because such method would have been a product of ordinary skill and common sense as any ordinary person would have been capable of n reading and utilizing the information presented by Stokes. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

26. **Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stokes et al. (WO 00/47212; published 08/17/2000) as applied to claims 21, 23, 24, 27, 28 and 31-33 above, and further in view of Seibert et al. (US 5972986; published 10/26/1999).**

27. Stokes fails to teach oxalipatin as being a platinum-based antitumor agent.

28. Saibert cures this deficiency. Saibert teaches a variety of antineoplastic agents including cisplatin, carboplatin, as well as oxaliplatin (see column 13, lines 15-30).

29. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Stokes and Seibert with a reasonable expectation for success in arriving at a method of treating cancer wherein the platinum antitumor agent is oxaliplatin. One would have been motivated to use oxaliplatin in the method of treating cancer taught by Stokes with a reasonable expectation that the use of oxaliplatin would reduce

the size of the cancer. Its use is especially obvious in view of Stokes specifically calling for use of platinum based antitumor agents. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

30. **Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Stokes et al. (WO 00/47212; published 08/17/2000) as applied to claims 21, 23, 24, 27, 28 and 31-33 above, and further in view of Oncology channel (http://www.oncologychannel.com/lungcancer/types.shtml, .pdf provided; published 08/24/1999).**

31. Stokes fails to specificy the lung cancer as being non-small cell lung cancer (or large cell lung cancer)

32. Oncology channel teaches a variety of different lung cell types. Of those listed, non-small cell lung cancer is disclosed.

33. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Stokes and Oncology channel with a reasonable expectation for success in arriving at a method of treating cancer wherein the lung cancer is non-small cell lung cancer. Stokes teaches that lung cancer may be treated using their compounds. While Stokes does not specify non-small cell lung cancer, its selection from the various types of lung cancer would not have been difficult given that lung cancers exist as two groups: small cell and non-small cell. Any person of ordinary skill would have been capable of picking one of the two (i.e. non-small cell) for treatment with the method of Stokes with a reasonable expectation in

the cancer being treated. Therefore, the invention as a whole is *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in absence of evidence to the contrary.

Conclusion

34. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

35. A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

36. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kyle A. Purdy whose telephone number is 571-270-3504. The examiner can normally be reached from 9AM to 5PM.

37. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau, can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

38. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Kyle Purdy/
Examiner, Art Unit 1611
December 17, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643